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1614 RCE #

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REQUEST FOR CONTINUED EXAMINATION (RCE) TRANSMITTAL

Subsection (b) of 35 U.S.C. § 132, effective on May 29, 2000 provides for continued examination of a utility or plant application filed on or after June 8, 1995.
See The American Inventors Protection Act of 1999 (AIPA)

Application Number: 09/555,026	
Filing Date: January 18, 2002	
First Named Inventor: Tadashi Mukai	
Group Art Unit: 1614	RECEIVED
Examiner: Donna A. Jogoe	
Attorney Docket Number: **6854-11**	FEB 1 2 2004
Attorney Customer Number: 22,852	TECH CENTER 1600/2900

This is a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114 of the above-identified application.

Note: 37 C.F.R. § 1.114 is effective on May 29, 2000. If the above-identified application was filed prior to May 29, 2000, applicant may wish to consider filing a continued prosecution application (CPA) under 37 C.F.R. § 1.53(d) instead of a RCE to be eligible for patent term adjustment provisions of the AIPA. See "Changes to Application Examination and Provisional Application Practice," Interim Rule, 65 Fed. Reg. 14865 (March 20, 2000). Off. Gaz. Pat. Office 47 (April 11, 2000), which established RCE practice.

1. **Submission required under 37 C.F.R. § 1.114: Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs therwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, application must request non-entry of such amendment.**

   a. ☐ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

      i. ☐ Consider the arguments in the Appeal Brief of Reply Brief previously filed on [Date] _____.

      ii. ☐ Other _____

   b. ☒ Enclosed:

      i. ☒ Amendment/Reply

      ii. ☐ Affidavit(s)/Declaration(s)

      iii. ☐ Information Disclosure Statement

      iv. ☐ Other _____

2. Miscellaneous

   a. ☐ Suspension of action on the above-mentioned application is requested under 37 C.F.R. § 1.103(c) for a period of [number] months. (Period of suspension shall not exceed 3 months; fee under 37 C.F.R. § 1.17(i) required.)

   b. ☐ Other _____

3. Fees

   a. ☒ The filing fee is calculated as follows:

      i. ☒ $770.00 RCE fee required under 37 C.F.R. § 1.17(e)

      ii. ☒ Petition for extension of time for (three Months) $950.00

      iii. ☐ Other _____

   b. ☒ Check in the amount of $1720.00 enclosed.

   c. ☒ The Commissioner is authorized to charge any deficiencies in the filing fees, or credit any overpayments to Deposit Account No. 06-0916.

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Signature of Applicant, Attorney, or Agent Required

Name: Arthur S. Garrett	Reg. No.: 20,338
Signature:	Date: February 2, 2004

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PATENT
Customer No. 22,852
Attorney Docket No. **6854-11**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Tadashi Mukai et al.

Application No.: **09/555,026**

Filed: January 18, 2002

For: Cilostazol Preparation

Group Art Unit: 1614

Examiner: Donna A. Jagoe

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

REPLY TO OFFICE ACTION

In reply to the Office Action mailed August 1, 2003, the period for response having been extended to February 1, 2004 (a Sunday) by a request for extension of three months and fee payment filed concurrently herewith, please respond to the above-identified application as follows:

Attachments to this response include: The Merck Index, 13th Edition - 3 pages
Arzneimittel-Forschung/Drug Research 35(II), 7a, 1117-1123 (1985).

RESPONSE

Claims 1, 4, 7-10, 12-14, 20, 21, 23-26 and 29-31 are pending in this application.

Main claim 1, from which all other claims depend directly or indirectly, relates to a cilostazol preparation having a capability of dissolving cilostazol even at the lower portion of the digestive tract which comprises incorporating a fine powder of cilostazol having an average particle diameter of 10 μm or less as an active ingredient into a surfactant as a dispersing and/or solubilizing agent. A typical surfactant is an alkyl sulfate salt such as sodium lauryl sulfate. Applicants found that such a composition has significantly improved dissolvability, particularly in the lower digestive tract.

Cilostazol is produced by a chemical synthesis resulting in a bulk cilostazol powder typically having an average particle diameter of 20 μm or so. This powder has a low absorbability in the lower digestive tract and its absorbability is not improved even with a dispersing and/or solubilizing agent. See page 4, lines 4-9 of the specification. Up to now cilostazol powder having an average particle diameter less than about 20 μm has not been known in the art and particularly not a powder having an average particle diameter of 10 μm or less.

In the Office Action, the Examiner rejected claims 1, 4, 7-10, 12-14, and 29-31, all relating to a cilostazol preparation, under 35 U.S.C. § 102(b) for being anticipated by Takada et al. (US Patent No. 6,117,455), hereafter Takada. Claims 20, 21, and 23-26 all relating to a sustained release preparation containing the cilostazol preparation of the previous claims and a sustained release coating material were rejected under 35 U.S.C. § 103(a) for being obvious over Takada in view of WO97/48382. The withdrawal of the rejection of the claims in view of Patel et al. as set forth in the Office

Action of October 28, 2002 is appreciated. However, it is believed the present claims are also patentable over the newly cited reference to Takada in view of the following.

Takada relates to a sustained-release microcapsule containing an amorphous water-soluble pharmaceutical agent having a particle size of from 1 nm-10 μm in a solution of a polymer in an organic solvent, wherein the pharmaceutical agent is dispersed in an aqueous phase, in an amount of from 0.001-90% (W/W) of the agent in a solution of the polymer, the polymer having a wt. avg. molecular weight of from 2,000-800,000. Cilostazol is one of a large number of pharmaceutical agents disclosed as examples of the agent, (see column 6, line 19 of Takada). Sodium laurate as an emulsifying agent can be included in the composition, (see column 12, line 17 of Takada). The Examiner therefore believes that the disclosure of cilostazol as a possible pharmaceutical agent, which agent has a particle size of less than 10 μm in an organic solvent that can contain sodium laurate, anticipates applicants' noted claims.

However, Takada specifically requires that the pharmaceutical agent used be "a water-soluble drug." See, for example, column 1, lines 33-35 where it is stated that the "main object of the present invention is to provide a sustained release microcapsule that has a high entrapment of a water-soluble drug . . . ." See also column 2, lines 43-44 where it is stated that the "physiologically active substance (i.e., the pharmaceutical agent) is not specifically limited so long as it is amorphous and water-soluble." (Emphasis added). Moreover, the term "water-soluble" is defined by Takada to mean that not less than 1 gram of the agent is soluble in 100 ml of water at 20°C. Preferably the agent is "readily soluble in water." See column 2, lines 32-42 of Takada.

While many of the pharmaceutical agents disclosed in Takada may be readily soluble in water, and presumably at least all of the agents set forth in the Examples 1-10 are, cilostazol is not water-soluble, and in fact, is practically water-insoluble.

In support of applicants' position, enclosed is a copy of page 395 of the 13th Edition of The Merck Index which indicates that cilostazol is practically insoluble in water. Moreover, according to the Japan Pharmacopeia, cilostazol is also considered "practically insoluble" in water and is said to have a solubility of only 0.000334 W/V%. See Table 5 on page 193 of Arzneimittel-Forschung/Drug Research 35(II), 7a, 1117-1123 (1985), a copy of which is also enclosed. Clearly this does not meet the requirement in Takada that at least one gram of the pharmaceutical agent be soluble in 100 ml of water. It is further noted that while Takada might have mentioned cilostazol as a pharmaceutical agent, there are no specific examples in the reference of a sustained release microcapsule containing cilostazol.

It is submitted therefore that because Takada clearly requires the use of only a water-soluble pharmaceutical agent, and cilostazol is not, the disclosure of cilostazol in the reference is an inoperable example of a suitable pharmaceutical agent. Thus, one skilled in the art reading Takada and knowing that cilostazol is not soluble in water, would know that cilostazol was not suitable for use in the disclosed invention even though it is mentioned as a possible agent.

Since applicants have clearly demonstrated by a preponderance of the evidence that Takada, as it is being applied by the Examiner to reject the claims, is inoperable, it therefore cannot be said to teach cilostazol having a particle size of 10 μm or less. See

M.P.E.P. 716.07. Withdrawal of the rejection of claims 1, 4, 7-10, 12-14, and 29-31 for being anticipated by Takada is therefore requested.

WO97/48382 may teach the combination of cilostazol and a sustained release material, but it like Takada fails to teach the claimed particle size of the cilostazol. Thus it is submitted that claims 20, 21, and 23-26 cannot be considered obvious over Takada in view of WO97/48382 either.

It is believed claims 1, 4, 7-10, 12-14, 20, 21, 23-26, and 29-31 are in condition for allowance.

In view of the foregoing remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: February 2, 2004

By: _____
Arthur S. Garrett
Reg. No. 20,338

Attachments: The Merck Index, 13th Edition - 3 pages
Arzneimittel-Forschung/Drug Research 35(II), 7a, 1117-1123 (1985).